

**MUTANTS OF THYROID STIMULATING HORMONE
AND METHODS BASED THEREON**

Abstract of the Disclosure

The present invention is based upon the discovery that mutant α subunits
5 and mutant β subunits each comprising amino acid substitutions relative to the wild type
can be produced and assembled to form a mutant TSH heterodimer or TSH analog that
possesses higher bioactivity in vitro and longer half life in vivo. Accordingly, the present
invention provides methods for using mutant TSH heterodimers, TSH analogs, fragments,
and derivatives thereof for treating or preventing diseases of the thyroid, in particular
10 thyroid cancer. The invention also relates to methods of diagnosis, prognosis and
monitoring for thyroid-related functions. Pharmaceutical and diagnostic compositions,
methods of using mutant TSH heterodimers and TSH analogs with utility for treatment
and prevention of metabolic and reproductive diseases are also provided.

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